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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,330	10/22/2003	Istvan Boldogh	265.00390101	1384

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EXAMINER	
KAM, CHIH MIN	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 09/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/691,330	BOLDOGH ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *16-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-15* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/18/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Status of the Claims

1. Claims 1-23 are pending.

Applicants' amendment filed July 18, 2005 is acknowledged. Applicants' response has been fully considered. Claims 1, 5, 6, 7 and 12 have been amended, and new claim 24 has been cancelled. Claims 16-23 are non-elected inventions and withdrawn from consideration. Therefore, claims 1-15 are examined. This application contains claims 16-23 drawn to an invention nonelected with traverse in the response filed March 8, 2005. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawn Informalities

2. The previous objection to the specification regarding web address is withdrawn in view of applicants' amendment to the specification in the amendment filed July 18, 2005.

Withdrawn Claim Objections

3. The previous objection to claims 6-7 regarding the recitation of non-elected sequences in the claims, is withdrawn in view of applicants' amendment to the claim, and applicants' response at page 9 in the amendment filed July 18, 2005.

Withdrawn Claim Rejections - 35 USC § 112

4. The previous rejection of claims 1-15, under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicants' amendment to the claim, and applicants' response at pages 10-11 in the amendment filed July 18, 2005.

Maintained Informalities

The disclosure is objected to because of the following informalities:

5. In the declaration, the instant application claims the benefit of a PCT Application No. PCT/US03/33423 under 35 U.S.C. 120, however, the specification does not indicate whether the instant application is a continuation, divisional or CIP of the PCT application in the continuation data at page 1, lines 11-13 of the specification. Appropriate clarification is required.

Response to Arguments

Applicants indicate while the Declaration submitted November 3, 2004, includes a priority claim to PCT US 03/33423, filed October 22, 2003, this priority claim is not included in first sentence of the application or on the application data sheet, and this application does not claim priority to PCT US 03/33423, filed October 22, 2003.

Applicants' response has been considered, however, the argument is not found persuasive because the Declaration has indicated the instant application claims the benefit of a PCT Application No. PCT/US03/33423 under 35 U.S.C. 120, which should be consistent with the continuation data cited in the specification.

Maintained Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-5 and 7-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting apoptosis or reducing DNA damage in a cell, the method comprising contacting the cell with an effective amount of an

apoptosis inhibitor selected from the group consisting of colostrinin, a constituent peptide of colostrinin consisting of SEQ ID NOs:1-7 or 8, and combination thereof, does not reasonably provide enablement for a method of inhibiting apoptosis or protecting against DNA damage in a cell, the method comprising contacting the cell with an effective amount of an apoptosis inhibitor, wherein the apoptosis inhibitor is an active analog of a constituent peptide of colostrinin consisting of SEQ ID NOs:1-7 or 8, and wherein the active analog comprises a peptide having an amino acid sequence with at least 15 percent proline and having at least 70 percent sequence identity to a constituent peptide of colostrinin of SEQ ID NO:1-7 or 8, and wherein the active analog inhibits apoptosis in a cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-5 and 7-15 encompass a method of inhibiting apoptosis or protecting against DNA damage in a cell, the method comprising contacting the cell with an effective amount of colostrinin, a constituent peptide of colostrinin of SEQ ID NO:1-8, an active analog of the constituent peptide, and combinations thereof. The specification, however, only discloses cursory conclusions (page 3, lines 8-27), which state that the present invention provides a method of inhibiting apoptosis or protecting against DNA damage in a cell comprising contacting the cell with colostrinin, a constituent peptide, an active analog or combinations thereof, where the active analog is an active analog of a constitute peptide of colostrinin selected from the group of SEQ ID NO:1-34, and the active analog comprises a peptide having an amino acid sequence with at least about 15% proline and having at least 70 % structural similarity to one or more constituent peptides of colostrinin. There are no indicia that the present application

enables the full scope in view of the use of colostrinin, a constituent peptide thereof, an active analog thereof, and combinations thereof in the claimed method as discussed in the stated rejection. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the active analogs of the constituent peptides of colostrinin of SEQ ID NO: 1-8, which are not adequately described or demonstrated in the specification.

(2). The presence of absence of working examples:

The specification has shown inhibition of 4HNE (4-hydroxy-2-nonenal)-induced or UV-irradiation-induced apoptosis by colostrinin in PC12 cells (Examples 7-8; Figs 8-9), however, there are no working examples indicating the apoptosis-inhibiting activity or the activity of protecting against DNA damage by active analogs of constituent peptides.

(3). The state of the prior art and relative skill of those in the art:

The related art indicates colostrinin and its fragment are useful for treating disorders of central nervous system, neurological disorders and neurodegenerative disorders and a composition comprising colostrinin or its constituent peptide is prepared (page 1, lines 25-33 of the instant application; WO 98/14473), and considerable evidence has indicated increased

oxidative stress may play a role in the pathogenesis of neuron degeneration and death in the neurodegenerative disorders (Markesbery, Free Radical Biology & medicine 23, 134-147 (1997)). However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the structures of active analogs of various constituent peptides of colostrinin to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass a method of inhibiting apoptosis or protecting against DNA damage in a cell, the method comprising contacting the cell with an effective amount of colostrinin, a constituent peptide of SEQ ID NO:1-8, an active analog of the constituent peptide, and combinations thereof. However, the specification has not provided sufficient teaching on identification of various active analogs for constituent peptides of SEQ ID NO:1-8, it is unpredictable regarding the structures of these active analogs and their effects in inhibiting apoptosis or protecting against DNA damage in a cell.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims encompass a method of inhibiting apoptosis or protecting against DNA damage in a cell, the method comprising contacting the cell with an effective amount of colostrinin, a constituent peptide of SEQ ID NO:1-8, an active analog of the constituent peptide, and combinations thereof. The specification shows inhibition of 4HNE-induced or UV-irradiation-induced apoptosis by colostrinin in PC12 cells (Examples 7-8; Figs 8-9), and indicates the active analogs of constitute polypeptides of colostrinin include polypeptides having

amino acid sequences with at least 15% percent proline or have at least 70% structural identity to colostrinin or one or more of its constituent peptides (page 11, lines 1-16). However, the active analogs with certain structural characteristics such as at least 15% percent proline and have at least 70% sequence identity to the constituent peptide still encompass many variants, the specification has not disclosed any particular structure to function/activity relationship among the variants. Without guidance on structure to function/activity, one skilled in the art would not know which residues in the sequence are essential for function/activity and how to identify a functional polypeptide. Since the specification does not provide sufficient teachings on the identification of various active analogs of the constituent peptide, it is necessary to have additional guidance and to carry out undue experimentation to identify the active analogs in the claimed methods.

(6). Nature of the Invention

The scope of the claims includes many structural variants for active analogs of constituent peptides of colostrinin, but the specification does not provide sufficient teachings on the identification of active analogs in the claimed method. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not demonstrate the variants associated with the claimed methods, and the teachings in the specification are limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to identify the active analogs of the constituent peptides of colostrinin in the claimed methods.

Response to Arguments

Applicants indicate as amended, the structure of the constituent peptides of colostrinin and the active analogs of a constituent peptide of colostrinin in claims 1-5 and 7-15 is adequately defined. Specifically, the constituent peptides of colostrinin are selected from the group consisting of SEQ ID NO: 1-8 and the active analogs of a constituent peptide of colostrinin have "an amino acid sequence with at least about 15 percent proline and having at least about 70 percent structural similarity to a constituent peptide of colostrinin selected from the group consisting of SEQ ID NO: 1-8", where guidance for active analogs of constituent peptides have been provided in the specification (page 12), thus one of skill in the art is able to make and use these peptides (pages 9-10 of the response).

Applicants' response has been fully considered, the argument is found persuasive regarding the constituent peptides of SEQ ID NO:1-8. However, the argument is found not persuasive regarding the active analogs of the constituent peptides of SEQ ID NO:1-8 because although the specification disclose certain structural characteristics of the active analogs such as at least 15% percent proline and have at least 70% sequence identity to the constituent peptide, the active analogs still encompass many variants, and the specification has not described any particular structure to function/activity relationship among the variants. Without guidance on correlation of structure to function/activity, one skilled in the art would not know which residues in the sequence are essential for function/activity and how to identify a functional polypeptide. Therefore, without undue experimentation to identify the active analogs, one skilled in the art would not be able to make and use these peptides.

New Claim Rejections - 35 USC § 112

7. Claims 1-5 and 7-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 1-5 and 7-15 are directed to a method of inhibiting apoptosis or protecting against DNA damage in a cell, the method comprising contacting the cell with an effective amount of colostrinin, a constituent peptide of colostrinin, an active analog of a constituent peptide of colostrinin, and combinations thereof, wherein the constituent peptide of colostrinin is selected from the group consisting of SEQ ID NO:1-8, and wherein the active analog of a constituent peptide of colostrinin comprises a peptide having an amino acid sequence with at least 15 percent praline and having at least 70 percent sequence identity to a constituent peptide of colostrinin of SEQ ID NO:1-7 or 8. While the specification discloses SEQ ID NO:4 has amino acid sequence LFFFLPVVNVLP and SEQ ID NO:8 has amino acid sequence LKPFPKLKVEVFPFP (page 10, lines 1-3; sequence listing), the specification does not indicate LFFFLPVGVLP is SEQ ID NO:4 and LKPFPCKVEVFPFP is SEQ ID NO:8 as cited in the claims. The lack of description of SEQ ID NO:4 being LFFFLPVGVLP and SEQ ID NO:8 being LKPFPCKVEVFPFP, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Claim Objection

8. Claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

9. Claims 1-5 and 7-15 are rejected, and claim 6 is objected to.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D. CMK
Patent Examiner

CMK
September 23, 2005

KATHLEEN M. KERR, PH.D.
SUPERVISORY PATENT EXAMINER